POSTOPERATIVE PNEUMONIA, WITH EXPERIMENTS UPON ITS PATHOGENY.

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SINCE this is one of the few subjects which is not adequately covered in medical literature, and since postoperative pneumonia has almost invariably been attributed to the anæsthetic, no apology is needed for inviting the attention to a brief discussion of the subject, to views taken at a new angle, and to a few experiments which may have some clinical significance.

No complication is more dismaying to the surgeon or more disastrous to the patient, and it would seem that any light which may be shed upon its etiology or suggestions as to its prevention should be most welcome. Occasionally, after an operation performed with the requisite speed and technical skill, the temperature rises with an initial chill, increased pulse-rate, and systemic depression which at first suggest sepsis, and show for their only cause a percussion area on the chest, a few moist or crepitant râles, all progressing rapidly to a fatal end.

What, then, may be the causes of this complication? What is there in the surgical state which renders a patient more susceptible to pulmonary infection at this particular time? Is it the ether, the reduced condition of the system caused by those factors which make an operation necessary,—a cold operating table with cold water for "washing up"? Is surgical pneumonia different from any other? Did pulmonary disease exist before a pneumonitis developed, or was there a particular opportunity for an infection? All these questions are interesting and important in the *rationale* of an individual case.

Of especial interest, however, is the possibility of a pneumonia already existing in a latent state or in a typical form. Knowing as we now do the great frequency of these forms of

pneumonia as contrasted with the frank, undoubted variety, and the great commonness of cases which have at first but little elevation of temperature and practically no physical signs, is it at all remarkable that occasionally consolidation shows itself a few days after an operation of no particular severity or danger? Again, it is impossible to overlook the element of chance in reviewing the likelihood of pneumonia after an operation. We do not as yet know whether the prevalence of pneumonia at certain seasons is due to climatic changes, a state of particular virulence of the bacteria, or both; and it seems that nothing could be more unreasonable than to ascribe to the anæsthetic a disease quite prevalent among those not affected with surgical ailment.

Statistics are of but little value in an inquiry into the etiology of this disease. That different observers found it to occur once in a certain number of cases throws no light whatever on the subject further than to show that it occasionally does occur after an operation. Prescott, in reviewing 40,000 cases at the Massachusetts General Hospital, found but three cases; Silk reports thirteen in 5000 surgical cases, and Anders, in a review of 12,842 surgical cases, found thirty. Kelley has seen eight cases in 1800 administrations of various anæsthetics, and is of the opinion that coryza as well as bronchitis predisposes to the complication. The writer, in a necessarily limited experience, has a knowledge of five cases, and is of the opinion that the condition is of much greater frequency than these reviews would indicate.

Various vasomotor changes result from the necessary circumstances of an operation. Conspicuous among these is the exposure of the body surface to a temperature of 70° F. or under, cleansing solutions may be cold, and if the clothing be wet the patient is swathed in a cold poultice at a time when he should be protected from such an influence. We have in these precisely the same factors which are accounted as causes of colds, respiratory and the so-called rheumatic disorders with the added changes in the peripheral circulation incident to the anæsthetic. These vasomotor changes are prime features in surgical shock,

and for this reason a warm bed with heaters should await the patient, and be maintained until circulatory equilibrium has become re-established. If the operation be upon a patient reduced by long-continued illness, external or concealed hæmorrhage, or if there is a possibility of collapse or death on the table, everything should be done to maintain the body temperature. Among the various means to this end the hot-water mattress is of particular importance.

As to the ability of ether to produce pneumonitis, some affirm it, others deny it, but all dread it. For years the necessity of careful dosage in anæsthetics with the view of reducing shock, irritation, and vomiting to a minimum has been urged; and, although it would seem that the application of these principles would lessen the possibility of postoperative bronchitis or pneumonia, we have as yet no convincing data that ether is a prime or direct cause of pulmonary complications. Indeed, it is claimed by some that pneumonia occurs quite as frequently when local anæsthesia is used. Experimentally, it is not at all easy to produce pneumonia. Aufrecht could not produce it in healthy rabbits by subcutaneous or intrapulmonary injection of pneumonic sputum, and after an interesting series of experiments concludes that a pre-existing pathological lesion is necessary for the deposition and multiplication of pathogenic bacteria. Grave pathological conditions (abscesses) and death may be caused, but not pneumonia. That bacteria are found in the bronchioles, and even in the finest ramifications of the air-passages under certain conditions, cannot be doubted, for Klipstein found that, although they were normally absent from the trachea, bronchi, and lungs of cats, dogs, and rabbits, they might be found in abundance after etherization. In the experiments of Lindemann, carmine was introduced into the mouths of rabbits, and after the animals had been etherized, particles were found in the smaller ramifications of the bronchi, having been carried there by the violent inspiratory efforts incident to the etherization. The writer also finds bacteria in the lungs of healthy rabbits.

It is fair to presume, however, that a theoretically perfect

epithelium is able to resist the ordinary invasions of bacteria: and it seems reasonable to suppose that any damage to the tissue would render the individual more susceptible.

Surgical pneumonia then may be divided into two classes, —one in which infectious particles are drawn into the lungs by the violent inspiratory efforts incident to anæsthesia, the other in which organisms of particular virulence find soil suitable to their growth and multiplication.

I have the honor of presenting a brief account of a few experiments upon the irritant effects of ether. It is a fundamental principle in pathology that a perfect tissue is less liable to infection or other degenerative changes than one previously injured or diseased. Cancer invades abraded and cicatricial tissue, the diphtheria bacillus finds a fruitful soil in the catarrhal pharynx, pneumonia and bronchitis more quickly attack those with pre-existing pulmonary lesions, and sepsis attacks abraded rather than unbroken surfaces. Without elaboration of the reasons why this is so, it may be stated that any evidence that the inhalation of a vapor produces structural changes in the lungs, thereby opening increased possibilities for bacterial lodgement, may serve as an explanation of postoperative phenomena. The inhalation of silicious particles causes minute wounds upon which tuberculosis may develop; perhaps the minute hæmorrhages which we shall see take place in the lungs in prolonged or careless anæsthesia, may serve for the subsequent development of pneumonia if the specific bacteria be brought to such lesions before they are healed. With this in mind, I have made a number of experiments with rabbits to see if possible whether the irritant effects of ether reach down into the lung tissue, or are confined to the larger bronchial tubes, and whether etherization increases susceptibility to pneumonic infection. Securing first a normal lung by decapitating the rabbit, for suffocation or brain puncture causes engorgement of the pulmonary vessels with rupture of the alveolar capillaries, sections were prepared by fixing and hardening in Zenker's solution and alcohol and embedded in paraffin. Sections were for the most part five microns in thickness and transverse to the tubules. The next

step was to observe the effect of ordinary etherization on the rabbit's lung, and to this end ether was given by an inhaler for half-hour periods on three successive days, the lung being then prepared for observation as that of the control normal rabbit.

In order to see if a normal rabbit would acquire pneumonia if given ample opportunity, it was caused to inspire an atmosphere saturated with the diplococcus pneumoniæ, and to ascertain if a rabbit previously etherized was more susceptible, it was caused to inhale the same atmosphere.

To observe the effect upon a capillary net-work similar to that of the lung, the web of the frog's foot was made use of, and to learn the effect of ether itself on the lung it was injected directly into the lung tissue of the living animal by a hypodermic syringe.

I. *Effects of Ether on the Frog's Web.*—In observing the frog's web before, after, and during exposure to ether, it was found that the effects of liquid ether and its fumes were the same in kind, the former acting more quickly. Macroscopically, the foot presented the appearance of intense congestion, dark and livid. Microscopically, it was found that all circulation had ceased, the blood in the vessels having become stagnated and presenting a mass of corpuscles packed so closely as to seem homogeneous. The larger blood-vessels could be made out, their contour unaltered, but the smaller capillaries seemed identical with the tissue. After a time, however, if the ether be removed, the circulation gradually asserted itself, feeble impulses could be detected in the arteries, which then become larger in caliber, and little by little with increasing impulses the solidified mass becomes broken up and is fluid again. Nearly an hour is required to completely restore the circulation after five minutes' exposure of the foot to ether fumes. Immediately upon the appearance of the slightest circulation, leucocytes appear in the lumen of the vessels, proceeding from the perivascular tissue, and these associate themselves with the vessel wall, adhering to it in spite of the ceaseless impact of the red corpuscles in the blood stream. In a few minutes these have

formed a complete lining for the vessels, and gradually the contour of the individual corpuscles is lost and a new endothelium is formed. In occasional instances the capillary wall was ruptured, so that the corpuscles poured out in a broad stream unrestrained by lateral walls, forming a true subcutaneous hæmorrhage easily seen by the unaided eye. To show that these phenomena were not due to refrigeration from the evaporation of the ether, ice and ice water were applied to the frog's foot, but only a slowing of the blood current was observed. The restoration of the circulation after as brief an exposure as five minutes is not always complete; some of the vessels may remain clogged and never become cleared, others regain their function for a time, but later fill up with agglutinated reds. If the exposure is as long as ten minutes, the tissue is killed and the circulation entirely destroyed, and after a few hours the integument peels off in strips over the entire area of exposure. The tissues underneath are devoid of circulation, and in a few days the flesh sloughs off, leaving only the skeleton.

We may conclude, then, that in the frog's capillary web ether causes arrest of the circulation, rupture of the blood-vessels, and in general phenomena of an inflammatory and hæmorrhagic nature with death of the exposed tissue, and that these effects are specific to ether and not the result of refrigeration. And it is interesting to note how short an exposure will cause these changes. From these observations, it was predicted that the changes produced in the lungs, if any, would be of the nature of hæmorrhages, a surmise that was fully realized.

II. *Effects of Ether upon the Lung.*—When ether is injected into the lung tissue of a live rabbit, the animal emits a few frightened cries and gives a few struggles, after which it remains quiet. For three or four minutes there is slight disturbance of equilibrium, but at no time is there anæsthesia. Râles appear at once in the chest, and are observed with stethoscopes of various kinds, the Bowles being the most satisfactory. The respirations and heart are

greatly accelerated, being doubled in velocity and of the ratio of one to two. Ten minutes after the injection of five minims of ether the pupils react to light, ether can be detected in the expired air, the respirations are labored, and the nostrils dilated, giving the characteristic appearance of air hunger. After this there is but little change in the animal's condition until its death, which occurs some ten hours later; the pulse remains about 200, the respiration 100; there is diminished respiratory movement of the affected side, a percussion area can be made out over the site of the injection. The respiration is distinctly bronchial over this area, the râles being loud and of all grades, from small sibilant to noisy rhonchi.

Necropsy upon this animal shows the tissue around the site of injection to be a mass of hæmorrhagic tissue which is solid, sinks in water, and is of a dark red color. There is a large mass of clotted blood in the cavity, adherent to the lung tissue and evidently proceeding from it rather than from the chest wall. The other lung shows areas of ecchymosis, but is otherwise normal, and a tendency towards those features found nearer the site of injection.

Microscopically, it is found that the structure of the lung is so completely changed as to leave but little resemblance to the normal. As seen by the microphotograph (Fig. 2) there is hardly a vestige of normal lung tissue. Instead there is a homogeneous mass of agglutinated red blood-corpuscles dotted with nucleated cells which are leucocytes and cells from the alveolar walls. The more remote from the point of injection, however, the more normal does the tissue appear; and it is possible to select areas which can be recognized as lung tissue. Even in the other lung we find alveoli filled with hæmorrhagic exudate, thickened walls, and nucleated cells proceeding from them into the spaces. The exudate in this experiment is of two kinds,—one of broken-down lung tissue with connective-tissue cells closely packed together, the other of a hæmorrhagic nature, consisting of blood extravasation agglutinated into a finely granular homogeneous mass.

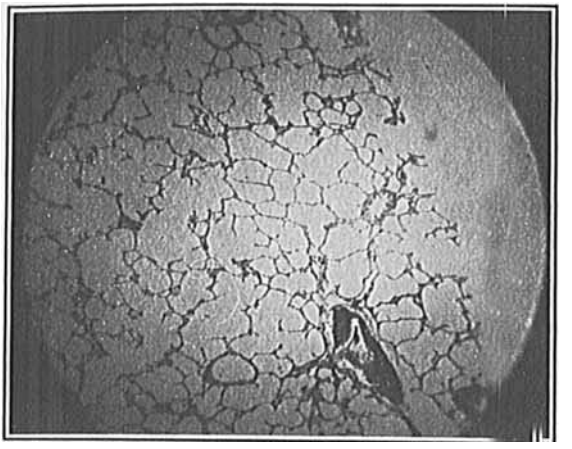

FIG. 1.—Section of lung of normal rabbit. × 87.

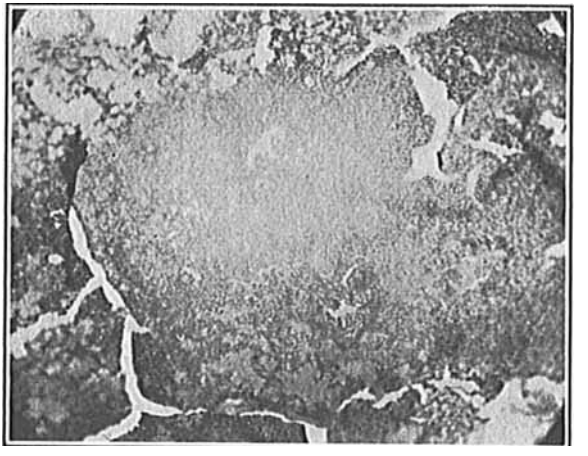

FIG. 2.—Section of rabbit's lung into which ether has been injected. Lung structure is completely lost; there are no vestiges of alveoli or walls; the almost homogeneous mass is composed of red and white blood-corpuscles with nucleated cells of the destroyed lung tissue.

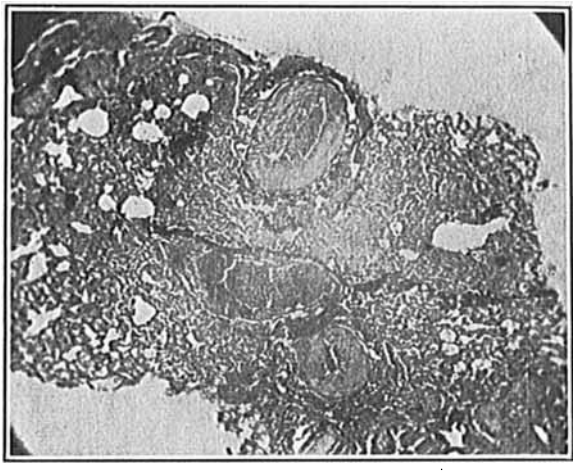

FIG. 3.—Section through hæmorrhagic area of an etherized rabbit. Showing only suggestions of alveolar structure, the blood-vessels having ruptured and the alveolar walls having become agglutinated. This section is longitudinal to the alveolar ducts.

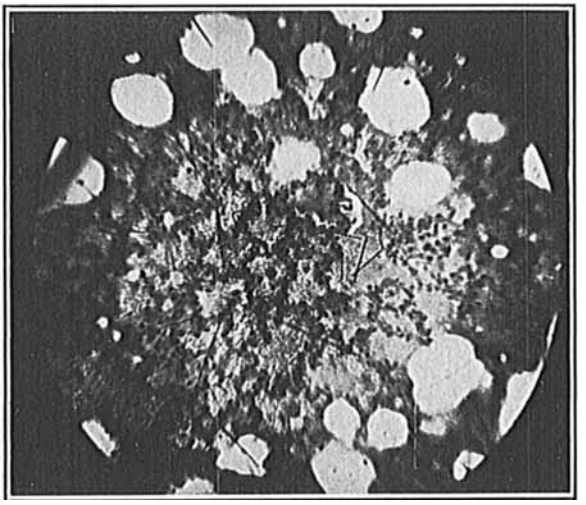

FIG. 4.—Etherized rabbit caused to inhale vaporized culture of pneumonia germs. Almost complete consolidation of the lung. The alveolar walls may be made out, but the spaces are filled with exudate. The walls are engorged, and reds may be seen proceeding from them.

III. *The Effects of Ether Anæsthetization.—Macroscopically*, the lung of a rabbit previously anæsthetized shows dark red mottlings which for the most part are superficial. These are distributed over the surface of the lung and comprise a third of its external area. These are the areas over which râles were most distinctly heard during the etherization. It was thought, inferred from the observation of the frog's circulation under ether, that these mottled areas were hæmorrhagic in their nature, and microscopic examination shows this to be the case. The alveoli are swollen and full of corpuscles, the bronchial tissue is congested, and in many cases the corpuscles may be seen proceeding from the tissue into the alveoli and peribronchial spaces (Fig. 3). Experiment readily shows the increased susceptibility of rabbits to the irritant effects of ether with successive etherizations, for when one is carefully anæsthetized râles appear in the chest in about a half an hour. If, then, this rabbit be undisturbed for two or three days and again anæsthetized, they appear in about fifteen minutes. A third anæsthetization causes râles and rhonchi to appear in five minutes or less. It is interesting to note, also, that the forcing or crowding of the anæsthetic causes these features to appear in a very much shorter time. Furthermore, it is found that the microscopic changes in the lungs vary from the condition of congestion of the alveoli to actual intra-alveolar hæmorrhages, according to the care taken in the etherization, very short etherizations causing but little change in the lungs.

IV. *Etherized Rabbit Plus Pneumonia Culture.*—To learn if a rabbit previously etherized would acquire pneumonia, or if an infection would have any effect upon the lesions caused by ether, one was etherized for half an hour on three successive days, and in the intervals it was caused to inspire an atmosphere laden with Fraenkel's diplococcus pneumoniæ. Cultures of this organism were very kindly furnished me by Dr. Augustus Wadsworth, of Columbia University, and were administered by diluting with water and vaporizing in an ordinary nebulizer. To avoid scattering the bacteria, the rabbit

was caused to inhale through an aperture in a box which closely fitted its nose, and the vapor was introduced through a small aperture at the opposite end. This animal was certainly ill, refused its food, and its rate of respirations was distinctly increased. No râles could be detected, and the respiratory murmur was slightly increased. There were no percussion areas.

Macroscopically, the lung presents all the features of that already described as incident to etherization, but all are advanced and intensified. Its surface is studded with areas of irregular outline of a dark reddish-brown color; the peribronchial tissue is almost black and nearly solid; parts of the lung do not crepitate and nearly sink in water, and the abnormal tissue is not superficial, but massive, extending deeply into the lung tissue.

Microscopically, the findings are most interesting and fairly well shown in the microphotograph (Fig. 4). In these sections we have all grades of pneumonitis, from mere congestion, with but slight change from the normal, to actual consolidation of lung tissue. Selected areas show the typical picture so often seen in croupous pneumonitis,—the alveoli preserved in outline, but completely filled with exudate, which in some cases rests upon a delicate reticulum. The areas around the bronchi show a marked degree of peribronchitis, and the lumen of the bronchi are for the most part filled with exudate. When stained by Gram's and other methods for bacteria and capsules, an organism is found which is identical in morphology and staining properties with that used in the experiment.

The significance of this experiment depends not only upon the findings of the preceding one, but also upon those in a

V. *Normal Rabbit caused to Inhale Culture.*—This animal, although it showed slight lassitude for three days, did not refuse its food, and showed no elevation of temperature or increase in respiration.

Macroscopically, the lungs showed no abnormality whatever. There was no mottling, no signs of hæmorrhage, no change in the normal crepitation.

Microscopically, the sections showed a thickening of the alveolar walls, but without consolidation of tissue, peribronchitis, or exudate of any kind. The bacteria used in the experiment was occasionally found in the alveolar spaces and walls. In this animal we have a nearer approach to the normal than any in the series, and it is quite easy to find areas which show no abnormalities whatever.

VI. Finally, with the idea of learning if complete resolution took place in the lung of an etherized rabbit not influenced by infection, one was etherized until râles appeared in abundance, and after two weeks this animal was killed. It was found that the lungs showed the hæmorrhagic areas partially resolved, but still distinct; and it was deduced that some time must elapse, in the rabbit at least, before the lung is again normal. It would be an interesting and practical problem to make a series of experiments along this line with a view of determining the amount of time required and the manner in which resolution takes place.

The following conclusions seem justifiable and may be defended:

1. Prophylaxis. Care in ether giving lessens shock and respiratory irritation, which reach their maximum when an unnecessarily large amount of ether is given.

2. The disinfection of the mouth and oropharynx by peroxide before operation is a rational precaution.

3. Adequate air space is of even greater importance in surgical wards than in medical.

4. A careful auscultation and percussion of the chest should precede every operation, and if there be signs of disease, operations of election should be postponed until the chest condition is more favorable.

5. A complete clinical record of all cases of postoperative pneumonia, together with a record of the previous state of the patient, is most desirable, and such records will in time greatly enrich our incomplete knowledge of the factors which predispose to the complication.

6. It is possible to demonstrate experimentally the lesions produced by suffocation and etherization, and the same philosophy which explains postoperative pneumonitis may be applied to that which occasionally follows poisoning by carbon monoxide and illuminating gas.